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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/613,903	07/11/2000	Heather J. Jordan	0942.4450001	1446

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EXAMINER

SISSON, BRADLEY L

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 12/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/613,903	Applicant(s) JORDAN, HEATHER J.	
	Examiner Bradley L. Sisson	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 43-57, 59-61, 63 and 64 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 43-57, 59-61, 63 and 64 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 19 November 2003 has been entered.

Specification

2. The amendment filed 09 May 2002 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material, which is not supported by the original disclosure, is as follows: The entire specification of US Patent Application Number 08/892,884, which was incorporated by reference. While applicant may be entitled to claim benefit of priority to the prior application, the disclosure of the '884 application cannot be incorporated by reference in the instant application via an amendment submitted post filing.

3. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 43-49, 51-57, 59-61, 63, and 64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision of *Vas-Cath Inc. v. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 USC 112, first paragraph, requires a “written description of the invention” which is separate and distinct from the enablement requirement. The purpose of the “written description” requirement is broader than to merely explain how to “make and use”; the “applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the “written description” inquiry, *whatever is now claimed*.

6. For convenience, claims 43 and 63, the only independent claims, are reproduced below.

43. (New) A composition comprising a plurality of double-stranded DNA fragments of different lengths, wherein fragments of each length are present in an amount that produces bands of substantially equal intensity after the composition is separated by gel electrophoresis and stained with a detectable label.

Art Unit: 1634

43. (New) A composition comprising a plurality of double-stranded DNA fragments of different lengths, wherein fragments of each length are present in an amount that produces bands of substantially equal intensity after the composition is separated by gel electrophoresis and stained with a detectable label.

For purposes of examination, claims 43 and 63 have been interpreted as encompassing a composition that is virtually limitless in range of sizes of fragments, both in terms of upper and lower limits, and also in terms of differences in sizes of fragments. A review of the disclosure, however, fails to find support for such a range of sizes. In support of this position, attention is directed to page 4, last paragraph, bridging to page 5 of the specification, *infra*.

Specifically, the invention relates to nucleic acid ladders or compositions wherein all or substantially all of the bands are substantially equal in intensity and/or wherein all or substantially all of the bands are substantially equal in relative mass. In a preferred aspect of the invention, the compositions or ladders are comprised of nucleic acid fragments in increments of about 1 Kb (kilobase = 1,000 bases or base pairs) (e.g., 1 Kb, 2 Kb, 3 Kb, 4 Kb, 5 Kb etc.) and one or more nucleic acid fragments smaller than 1 Kb (for example, in increments 10 bp, 20 bp, 30 bp, 40 bp, 50 bp, 60 bp, 70 bp, 80 bp, 90 bp, 100 bp etc. or any combination thereof); wherein substantially all of the fragments of the ladder or composition are substantially equal in intensity when detected by staining, and/or wherein substantially all of the fragments are substantially equal in relative mass.

Preferably, the nucleic acid ladders and compositions of the invention have two or more bands (preferably four, five, six, seven, eight or more bands) ranging from about 25 Kb to about 100 bp or smaller, preferably 20 Kb to 100 bp, more preferably 15 Kb to 100 bp and most preferably 12 Kb to 100 bp, although smaller ranges are contemplated by the invention.

7. While applicant fairly asserts that other embodiments may be obvious, and indeed are encompassed by the claims, a review of the disclosure, however, fails to reasonably suggest that applicant was in possession of other DNA ladders. It would appear that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written

Art Unit: 1634

description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

8. Claims 63 and 64 are also rejected under 35 USC 112, first paragraph, as it relates to the introduction of new matter into the claims. Claim 63, on purposes of examination, has been interpreted as encompassing fragments whose intensity variance is predicated on one band being “visibly brighter” than that of another. The aspect of one or more bands being “visibly brighter” has been interpreted as encompassing virtually any value, from a “just noticeable difference” to infinity. A review of the specification fails to find an adequate description of such bands so to reasonably suggest that applicant contemplated such breadth of scope, much less reasonably suggest that applicant was in possession of the full genus encompassed by the claims. Attention is also directed to page 14, first full paragraph, which discloses that the “highlight bands or fragments” have a mass of 3 times to 5 times that of the other bands or fragments.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Art Unit: 1634

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 43-56, 59-60, 63 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Life Technologies Catalogue (1995-1996).

12. Life Technologies Catalogue discloses for sale a variety of DNA ladders. As seen at page 14-2, the ladder can be comprised of repeating units of 10 bp, and starting from an oligonucleotide of only 10 bp and can go to and beyond 100 bp. Also seen for sale are DNA ladders that are based on repeating units of 50 bp, 100 bp, 123 bp, 1 kb, etc.

13. Life Technologies Catalogue discloses that the concentration of some fragments in some ladders has been adjusted so that certain desired marker(s) appear brighter than others (a limitation of claims 63 and 64). It is also readily apparent that the individual bands in the 1 kb ladder also appear to be at the same relative intensity in the photo of stained bands in a gel subsequent to electrophoresis (see page 14-4). As seen in the caption for the 1 kb ladder, the DNA fragments can be visualized when stained with ethidium bromide (a limitation of claim 55).

14. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have developed any of a variety of DNA ladders for use in an electrophoresis assay and to have adjusted the relative concentrations of the bands such that the intensities of any one

Art Unit: 1634

or all bands was the same or more intense than others as the ordinary artisan desired. In view of the well-developed state of the art, and the broad usage of such markers, the ordinary artisan would have been both highly motivated and would have had a most reasonable expectation of success.

15. Claims 57 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Life Technologies Catalogue 1995-1996 as applied to claim Claims 43-56, 58-60 and 62 above, and further in view of Lee (US patent 5,268,568).

16. See above for the basis of the rejection as it pertains to the disclosure of Life technologies Catalogue 1995-1996.

17. Life Technologies Catalogue 1995-1996 does not disclose the use of the dye mixture.

18. Lee discloses that just a dye mixture comprising bromophenol blue or xylene cyanol FF is routinely added to DNA samples to be subjected to electrophoresis.

19. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the DNA ladders of Life Technologies such that a dye comprising bromophenol blue was included given its common usage in electrophoresis of DNA samples.

20. In view of the commercial availability of DNA ladders, a kit comprising same would have been an obvious commercial expedient, requiring little, if any, additional effort on the part of the ordinary artisan.

Response to argument

21. At page 5 of the response received 19 May 2003 applicant asserts:

The Life Technologies Catalogue does not, as the Examiner asserts in paragraph 7 at page 3 of the Office Action, disclose compositions that produce bands of substantially the same intensity when separated by gel electrophoresis and stained. A careful examination of the DNA ladders on pages 14-2 through 14-4 of the Life Technologies Catalogue reveals bands of varying intensities within each ladder.

The above argument has been fully considered and has not been found persuasive. It is noted that the claimed composition does not preclude the presence of bands of greater or lesser intensity. It is further noted that there need be only two bands that are of “substantially equal intensity after the composition is separated by gel electrophoresis” (emphasis added).

Accordingly, there need be present only two bands that are of “substantially equal intensity.”

With the phrase “substantially equal intensity” not being defined, said phrase has been interpreted as allowing for significant variability between bands. Basis for this interpretation is found in the fifth definition of “substantially” as provided by *Merriam-Webster Dictionary*:

5 : being largely but not wholly that which is specified <a *substantial* lie>

A review of *Life Technologies Catalogue* readily finds that it does present such an image of bands and as such, the prior art does meet this limitation of the claims.

22. Assuming *arguendo* that the prior art does not teach such a limitation, a point that the Office does not concede, the prior art still would render the claimed invention obvious as the improvement, if there is any, would be the result of routine optimization, which cannot be a point of non-obviousness. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

Art Unit: 1634

Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In *re Dreyfus*, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; In *re Waite et al.*, 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In *re Swenson et al.*, 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; In *re Scherl*, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In *re Sola*, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; In *re Normann et al.*, 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; In *re Irmischer*, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In *re Swain et al.*, 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; *Minnesota Mining and Mfg. Co. v. Coe*, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; *Allen et al. v. Coe*, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

For the above reasons, and in the absence of convincing evidence to the contrary, the claims are rejected under 35 U.S.C. 103(a).

Conclusion

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978.

The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

24. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Art Unit: 1634

25. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

A handwritten signature in black ink, appearing to read "B. L. Sisson".

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS

11/30/2003